TITLE: Compressible Non-Articulating Disc Prostheses: A Review of Clinical and Cost-Effectiveness, Safety and Guidelines

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CONTEXT AND POLICY ISSUES

Treatment options for discogenic low back pain include both non-surgical and surgical options. Amongst the surgical options, spinal segment fusion has a long history and is often characterized as the surgical standard of care.[1] Fusion aims to reduce pain by eliminating motion at the level of the diseased disc or discs but long term outcomes are poor and complications are common.[1]

Total disc replacement (TDR), which involves replacing a diseased disc with an artificial disc, is an increasingly popular surgical alternative. TDR is intended to restore normal spinal movement while also preventing adjacent level disc degeneration which may be associated with the kinematic and biomechanical changes produced by fusion.[1] Studies suggest TDR is non-inferior to fusion, at least in the short term.[2,3]

Artificial discs have been under development and/or in use for more than 25 years.[3,4] Research and development activity appears to be intense as, in recent years, at least 20 lumbar prostheses were under development or in clinical trials.[5]

Although all artificial discs are intended to achieve the same ends, there is considerable heterogeneity in design. TDR prostheses can be classified by mode of anchorage, surface and friction couple design, constrained or unconstrained motion, location of the centre of movement and compatibility with magnetic resonance imaging (MRI).[2] Some sources further classify disc prostheses as uni-articulating, bi-articulating, or non-articulating based on the friction couple design but the distinction is uncommon and/or inconsistent in the literature.[5,6] Uni- and bi-articulating designs rely on a mechanical interface (e.g., ball and socket or a variant thereof) whereas non-articulating designs do not (e.g., elastomeric, deformable core).

Most existing discs, particularly articulating discs, do not replicate the elasticity of the native disc. Efforts have been underway to develop a new generation of devices, such as the M6-L (Spinal Kinetics, Sunnyvale, CA), which would more effectively mimic the shock absorption and flexural stiffness of a native disc.

TDR is an insured service in some Canadian jurisdictions. Although the M6-L is not yet licensed in Canada, surgeons are interested in its potential as an alternative to the ProDisc-L (Synthes Canada, Mississauga, ON) and A-MAV (Medtronic Sofamor Danek, Memphis, TN) prostheses, both of which are articulating discs.

Given the challenging history of lumbar surgery and the variation in kinematic and biomechanical properties across device designs, choice of an artificial disc represents a major clinical practice issue.

RESEARCH QUESTIONS

1. What is the clinical effectiveness of compressible non-articulating disc prostheses in adult patients with degenerative disc disease?
2. What is the evidence regarding the safety of compressible non-articulating disc prostheses in adult patients with degenerative disc disease?
3. What is the cost-effectiveness of using compressible non-articulating disc prostheses in adult patients with degenerative disc disease?
4. What are the guidelines associated with the use of compressible non-articulating disc prostheses in adult patients with degenerative disc disease?

KEY FINDINGS

Limited evidence from a single non-comparative study suggests the M6-L performs as intended and is safe and effective at 24-months follow-up. Larger sample size and longer follow-up will be required to confirm these preliminary findings.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 2), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to documents published between January 1, 2009 and February 14, 2014.

Selection Criteria and Methods

This review is based on a previously completed Rapid Response reference list addressing the same topic.[7] For that report, titles and abstracts were screened by a single review based on pre-determined criteria, and relevant articles were selected for inclusion. Full text articles of all the reference list citations were retrieved and assessed by a single reviewer. Final inclusion was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults with degenerative disc disease
Intervention	TDR utilizing compressible non-articulating disc prostheses including but not limited to the M6 prosthetic
Comparators	Untreated patients or lumbar TDR patients treated with articulating disc prostheses including but not limited to the ProDisc-L and A-MAV
Outcomes	Clinical and/or comparative effectiveness (e.g., quality of life, back pain, left and/or right leg pain) Range of motion Safety/adverse events Cost-effectiveness (including cost-utility, cost-benefit, cost-minimization analyses) Guidelines
Study Designs	Health technology assessments (HTA), systematic reviews (SR), meta-analyses (MA), randomized controlled trials (RCT), non-randomized studies, guidelines and economic evaluations

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1. Articles were also excluded if not written in English, if they were published before January 1, 2009, if they were duplicate publications of the same study, or if they were referenced in an included systematic review.

Critical Appraisal of Individual Studies

The literature search failed to identify any HTAs, SRs, MAs or RCTs. As such, no formal quality assessment tool was used to assess the single non-comparative study included in this review. . Nonetheless, key features of the included study, including statistical power, sample population, and potential sources of bias were examined and described.

SUMMARY OF EVIDENCE

Quantity of Research Available

The original literature search yielded 550 citations. After screening of abstracts from the literature search and other sources, 37 potentially relevant articles were reviewed in full text. One study addressed the M6-L artificial disc and is included in this review. The included study

addresses clinical outcomes and safety. No economic evaluations or device specific guidelines were identified. The PRISMA flowchart in Appendix 1 details the process of study selection.

Summary of Study Characteristics

One non-comparative study[8] was selected for inclusion in this review.

Study Design

The included study is described by the study authors as a multi-centre, single arm, prospective post-market registry and compared baseline values with 24-month follow-up outcomes.

Population

The study population included 45 patients completing 24-months follow-up post TDR with the M6-L artificial disc. The study group included 20 males and 25 females with a mean age of 44.6 years. Mean height and weight were 172.1 centimetres and 76.7 kilograms while mean body mass index was 25.8.

Interventions and Comparators

All patients underwent TDR with the M6-L implant. Thirty-one patients were treated at 1 level (i.e., had one M6-L device implanted), 13 were treated at 2 levels, and 1 patient was treated at three levels. All implants occurred between the L3 and S1 levels. There was no comparator.

Outcomes

The authors report clinical and radiological outcomes including: Oswestry Disability Index (ODI), Visual Analogue Scale (VAS) for back and leg pain, patient satisfaction, disc angle, anterior and posterior disc height, global range of motion (ROM), and index ROM.

Summary of Critical Appraisal

The study by Ritter-Lang *et al.*[8] exhibits a number of strengths including explicit inclusion and exclusion criteria and reliance on a relatively standardized set of validated outcome measures but serious limitations remain.

Limitations include the absence of a comparator group, the small sample size (n=45) and the short duration of follow-up (24 months). Despite explicit inclusion/exclusion criteria the risk of bias in patient selection or other deviation from the criteria must also be considered significant. The authors acknowledge deviating from the inclusion criteria by including a patient requiring treatment at 3-levels.

Lack of sub-group analysis may also constitute a limitation as other authors have suggested TDR outcomes may be impacted by duration of disease and number of levels treated.[9,10] The

study also suffers from the equivalent to 'loss-to-follow-up' in that more than 50% of the patient sample did not complete the radiological studies necessary to assess ROM. This is a significant issue in that preservation of motion is one of the chief goals of TDR surgery.

Finally, the study authors are silent on funding and conflict-of-interest issues, however, the lead author has been quoted in the M6-L manufacturer's press materials.[11]

Summary of Findings

1. What is the clinical effectiveness of compressible non-articulating disc prostheses in adult patients with degenerative disc disease?

   The results from the included study are presented in Table 2. Statistically significant improvements occurred on all measures except ROM, where small changes were detected but statistical significance was not reported. In addition, the ODI and VAS changes were large enough to be considered clinically important. Thirty-four patients completed a satisfaction survey and 88% described their condition as greatly improved and 97% (32 of 33) indicated they would undergo the surgery again. The authors describe the results as promising and consistent with those reported for other artificial discs most, if not all of which, are articulating prostheses.

Table 2: Reported Clinical and Radiological Outcomes[8]

	Baseline		24-months	
Measure	**n=**	**Value**	**n=**	**Value**
ODI	45	45.9±16.5%	45	19.7±19.3%, p<0.001
VAS back pain	45	7.0±2.0	45	2.5±2.6, p<0.001
VAS right leg pain	45	3.5±3.2	45	1.1±1.9, p<0.001
VAS left leg pain	45	3.9±3.1	45	1.7±2.7, p<0.001
Disc angle	45	11.4^0	37	18.3^0, p<0.0001
Anterior disc height	45	10.2±3.1mm	37	17.7±2.9mm, p<0.0001
Posterior disc height	45	3.9±1.6mm	37	7.6±1.9mm, p<0.0001
Global ROM	45	38.0^0	18	40.6^0
Index ROM	45	6.4^0	19	5.6^0

2. What is the evidence regarding the safety of compressible non-articulating disc prostheses in adult patients with degenerative disc disease?

   Ritter-Lang *et al.*[8] reported no procedural complications, revisions, or device-related adverse events in their patient population. No other studies specifically addressing the safety of compressible non-articulating lumbar disc prostheses were identified.

3. What is the cost-effectiveness of using compressible non-articulating disc prostheses in adult patients with degenerative disc disease?

   No economic studies of any kind were identified.

4. What are the guidelines associated with the use of compressible non-articulating disc prostheses in adult patients with degenerative disc disease?

   No guidelines specific to compressible non-articulating lumbar disc prostheses were identified.

Limitations

Notwithstanding the positive performance of the M6-L for some outcomes in the included study, the device remains unlicensed in Canada. Furthermore, it is unclear whether the reported results would be generalizable to the Canadian context. The study provides minimal information regarding the patient population and no information regarding the surgical setting or the overall experience of the surgical team. Long-term safety remains unknown although experience with other lumbar disc prostheses confirms that device failure can occur.[3] Cost implications are also unknown.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Currently available evidence offers little definitive guidance for decision-makers contemplating the adoption of the M6-L artificial disc. Further complicating decision-making are more general calls for caution regarding TDR for lumbar pain given non-superior outcomes and lack of long-term follow-up.[1,12]

The M6-L was first implanted in a human patient in February 2009, 3-years after the cervical variant of the disc (M6-C) was first used.[13] In total, more than 10,000 of the M6 devices have now been implanted.[14] Despite what appears to be significant uptake, four clinical studies have been published to date, with one addressing the M6-L[8] and three addressing the M6-C.[10,15,16] Together these studies present data on 182 M6 devices with a maximum follow-up of 24-months.

Although the M6 devices have been described as advanced generation prostheses capable of replicating the anatomic, physiologic and biomechanical properties of the native disc, reported outcomes are generally described as being consistent with, rather than superior to, other disc prostheses.[8,16] One study addressing the M6-C reported slightly less improvement than that documented with other established disc prostheses.[10]

Information regarding the *in vivo* wear properties of the M6 devices has not been published and some researchers suggest the device, at least in its cervical variant, is significantly stiffer in some motions than the natural disc.[15] This might impact the ability of M6 devices to prevent adjacent level disc degeneration, the chief promise of TDR. However, some authors, including TDR surgeons, describe this benefit as still largely theoretical while others indicate 10 to 15 years follow-up will be necessary to actually confirm the benefit.[2,16]

It may also be the case that improved prostheses will not be sufficient on their own to achieve the promised outcomes. Proper placement of the artificial disc is necessary to precisely

reconstruct disc function and current surgical approaches may not be keeping pace with the innovations in prosthetic design, thus limiting the benefit of advanced designs.[15]

Although the M6 devices are seen by some as a significant advance in prosthetic design and appear to be safe and effective in the short-term, the available evidence to support their use is limited. Further, the absence of evidence of superior outcomes must be weighed carefully against the performance of currently utilized prostheses for which more follow-up data is generally available. Virtually all sources cite the need for larger clinical studies with long-term follow-up. Given the array of disc prostheses and the role of surgeon choice in selecting a prosthesis it is likely long-term follow-up will only be accomplished within the framework of a surgical registry such as exists in Switzerland.[17]

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Appendix 1: Selection of Included Studies